

REMARKS

Claims 1-9, 11, 12, 16, 17, 23, 25-31 and 38 are currently active.

Claims 10, 13-15, 18-22, 24 and 32-37 have been canceled.

Claim 38 has been added. Antecedent support for Claim 38 is found in Claim 1, and page 2, lines 28 and 29 in regard to the specific cells listed.

Antecedent support for the amendments to the claims in regard to the limitation of the average straight line velocity is found in figure 3, and the limitation regarding "human" is found on page 33, line 3; page 1, line 15 and Claim 20.

The Examiner has made the restriction requirement final. Applicant has canceled the non-elected claims.

The Examiner rejected Claims 1-9, 12, 17 and 30 under 35 U.S.C. 112. Applicant has amended the claims to obviate this rejection.

The Examiner has rejected Claims 1-4, 7, 9, 11, 12, 17, 23 and 25-31 as being anticipated by Casey. Applicant respectfully traverses this rejection.

The “teaching” of Casey, “that it is well known in the art to add methyl cellulose ... to reduce motility,” is specifically dealing with biological motility of rapidly moving cells “including, for instance, infusoria, protists and other motile micro-organisms.” This motion is much more rapid and possibly of a different nature than that of lymphocytes and other cultured cells from multi-cellular organisms. One often cannot keep motile unicellular micro-organisms in the view field of the microscope because they move too rapidly. Convection or motion along a mild slope is not a significant problem here. And so this prior art knowledge referenced by Casey is not concerned with non-biological motion or with the undesirable effects of relatively slow influences on the biological motion of cultured cells from humans. Instead, it is specifically concerned with using methyl cellulose to slow rapid biological motion of cells such as protests and other motile micro-organisms. Casey also does not presume that very low concentrations of methyl cellulose would be effective for suppressing non-biological motion without significant suppression of the biological motion of cells such as lymphocytes.

Casey’s invention is to basically kill these cells with hydrofluoric acid in order to “immobilize” them without having to mix the solution mechanically. Apparently

hydrofluoric acid diffuses rapidly throughout the solution, and the malachite green provides staining enhancement. Neither the prior art nor the invention described by Casey relate to the problems with slow moving cells and non-biological motion.

(A fundamental difference may exist between the nature of the motion of protests such as infusoria in which the driving force is the rapid beating of cilia or a flagellum in the liquid, compared with lymphocytes, where the motion is so slow as to be practically not visible in real time and where the driving force seems to be the reshaping of the cell from the inside out with forward protrusion of the cell at the front.)

The Examiner has rejected Claims 1-9, 11, 12, 16, 17, 23 and 25-31 as being unpatentable over Froman and Casey. Applicant respectfully traverses this rejection.

The patent by Froman makes use of layers to provide a “barrier” or a means to “separate” more motile sperm from less motile sperm. Froman describes only the use of layers of different density that remain stable long enough to separate the sperm that can swim into the new layer from the original layer. The number of sperm that swim through this barrier or into the “barrier medium” is related to the average motility of the specimen and can be measured by various methods automatically. Froman mentions that the barrier medium could be of greater density and/or viscosity, but only descriptions of density layers are

provided in the examples. This is a fundamentally different type of application in comparison to the subject application. The separation of sperm is carried out over a time period of minutes because the rate of biological motility of sperm is much more rapid than that of lymphocytes.

Applicant includes a description of adding a small amount of methyl cellulose as a thin layer in initial experiments. This was effective for suppressing non-biological motion at the cell culture surface because the added methyl cellulose solution, which was more dense than the culture medium, covered the cells at the bottom on the plastic surface, where the desired effect occurred. Later experiments are described where applicant used methyl cellulose as a homogeneous additive to the culture medium with the same effective suppressive effect on non-biological motion. The layering approach of the initial experiments was not an exclusive approach; instead it was necessary to maintain a sufficient concentration of methyl cellulose at the surface, and subsequently applicant learned that this could most easily be accomplished by using a homogeneous solution. The suitability of a homogeneous solution further contrasts applicant's claimed invention from that of Froman, whose method relies upon establishment of a barrier between two layers of liquid with properties that maintain their separation.

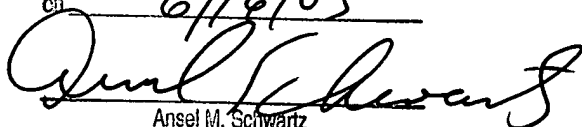
Applicant's claimed invention with lymphocytes and non-biological motion is one of much longer time intervals than the applications of Froman and Casey, because the rate of lymphocyte motility is much slower than that of sperm or micro-organisms. For example, "rapid progressive" sperm, a category of sperm motility, are classified with motility greater than 25 $\mu\text{m}/\text{sec}$. Lymphocytes, on the other hand, move on the average at speeds of 2 to 10 $\mu\text{m}/\text{min}$. Neither Froman nor Casey were concerned with biological motion of this order of magnitude and neither were confronting problems with gradual fluid motion observed, for example, over the course of 24-48 hour experiments.

Accordingly, the applied art of record, alone or together, does not anticipate or make obvious applicant's claimed invention.

In view of the foregoing amendments and remarks, it is respectfully requested that the outstanding rejections and objections to this application be reconsidered and withdrawn, and Claims 1-9, 11, 12, 16, 17, 23, 25-31 and 38, now in this application be allowed.

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Version with markings to show changes made to the claims

1. A method for analyzing a human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ by suppressing movement of the human cell caused by other than activity of the human cell itself comprising the steps of:

placing the human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution [having] containing a viscosity enhancement medium; and

measuring the motility of the human cell in the solution.

3. A method as described in Claim 1 wherein the viscosity enhancement medium is hyaluronic acid or chondroitin sulfate or cellulose ester or [poly sacharide] polysaccharide.

9. A method for analyzing a human cell by suppressing movement of the human cell caused by other than activity of the human cell itself comprising the steps of:

placing the cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution; and

measuring the motility of the human cell in the solution when there is no attachment to any surface of the cell involved.

11. A method for analyzing a human cell comprising the steps of:

placing the human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution having a viscosity of about 100-5000 [centipose] centipoise; and

performing two-dimensional or three-dimensional migration analysis on the cell in the solution.

12. A method for analyzing a cell comprising the steps of:

placing the cell in a solution having a viscosity of about 100-5000 [centipose] centipoise; and

analyzing migration of the cell in the solution which occurs without adherence to any surface.

17. A method for analyzing a human cell comprising the steps of:

placing the human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution having a viscosity of about 100-5000 [centipose] centipoise; and

measuring motility of the cell in the solution, where surface attachment by the cell to any surface is not utilized.

23. A method for analyzing a human cell by suppressing movement of the human cell caused by other than activity of the human cell itself comprising the steps of:

placing the human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution; and

placing methyl cellulose in the solution to reduce ambient motion of the human cell in the solution and eliminate convective motion.

25. A method for analyzing a human cell by suppressing movement of the human cell caused by other than activity of the human cell itself comprising the steps of:

placing the human cell in a solution; and

using methyl cellulose in the solution for stopping the effects of gravity on the human cell in the solution.

26. A method for analyzing a human cell by suppressing movement of the human cell caused by other than activity of the human cell itself comprising the steps of:

placing the human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution; and

using methyl cellulose in the solution for reducing or eliminating the effects of micro-turbulances due to thermal convection in the solution.

27. A method for analyzing a human cell comprising the steps of:

placing the human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution; and

introducing methyl cellulose in the solution for stopping motion of the cells due to mechanical movement of a plate on which the cells are disposed.

28. A method for analyzing a human cell comprising the steps of:

placing the human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution; and

introducing a viscous fluid having a viscosity of about 100-5000 [centipose] centipoise in the solution for stopping or reducing the effects of gravity on the cell.

29. A method for analyzing a human cell comprising the steps of:

placing the human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution; and

introducing a viscous fluid having a viscosity of about 100-5000 [centipose] centipoise in the solution for reducing the effects of micro-turbulences due to thermal convection.

30. A method for analyzing a human cell comprising the steps of:

placing the cell in a solution; and

introducing a viscous fluid having a viscosity of about 100-5000 [centipose]
centipoise in the solution for stopping motion of the cells due to mechanical movement of the plate.

31. A method for analyzing a human cell by suppressing movement of the human cell caused by other than activity of the human cell itself comprising the steps of:

placing the human cell having an average straight line velocity of between 0 and 10 $\mu\text{m}/\text{min}$ in a solution; and

using methyl cellulose or any viscous fluid to separate biological motility from ambient motility.